REMARKS

Claims 135-156 are pending in this application. Claims 1-134 are cancelled without prejudice or disclaimer.

Support for the claims can be found throughout the application. Applicants refer below to the paragraph numbers as published in 20040171740A1 to point out exemplary support:

Support for "contacting" and "controlled" can be found at paragraphs [106], [111], [115], [121], and [154]. Support for "mixing" can be found at paragraphs [15], [20], [23], and [196]. Support for "heating" and "workable" can be found at paragraphs [113] and [195-98]. Absence of chemical cross-linkers, irradiation or thermal cycling is discussed at paragraph [115]. Physical crosslinking is discussed at paragraph [132]. Anisotropy is discussed at paragraph [127]. Figures 21A and B are flow diagrams of exemplary methods of preparing injectable solutions and the resulting *in situ* hydrogels. Thetagels are discussed at paragraphs [30-35], [44-46], [50], [55], [65-67], [106-10], [129-32] and [167-76], and refer to when the Flory interaction parameter, which is dictated by temperature, solvent, and polymer is such that the polymer prefers to be with the solvent rather than itself. With the introduction of the second solution, the Flory interaction parameter increases, causing the polymer chains to move towards each other and overcome the 'solvation force,' causing localized phase separation, with regions having high concentrations of polymer (precursors to junction points) and regions with low concentrations (precursors to pores). If this localized phase separation

is controlled appropriately, the polymer chains can align to form crystalline junction points (crosslinks), which sets up a three-dimensional porous structure of polymer with some absorbed water, with the pores filled with water (*i.e.,* a hydrogel). If this phase separation occurs too quickly, the polymer precipitates out of solution (crashes out) before the polymer chains have an opportunity to form crystalline junction points or distinct precursor zones (junction points and pores), and consequently it will not form a hydrogel.

The claims are enabled and definite

Without acquiescing in any rejection, applicants have replaced the previous claims with claims 135-156. Support for the claims in the specification and an explanation of terms is set forth above. Applicants therefore submit that the Section 112 rejections are moot, and should be withdrawn.

The claimed invention is not taught or suggested by the prior art

The examiner has rejected the claims over various combinations of Hyon, Yamauchi, Tanihara, Ku, Yao and Okamura. Applicants have provided in depth arguments to distinguish these references, and therefore will summarize these arguments below.

- Ku, Yao, Hyon, and Okamura all require freezing step to form a hydrogel. See Ku *et al.* (see claim 1), Yao (see claim 1), Hyon (see claim 1) and Okamura (see the "constitution"). Yamauchi *et al.* states in its "constitution" that ionized radiation is used to form a gel. See Tests 2 and 3 of the Spiegelberg declaration (February 13, 2008). Therefore, to achieve injection of a hydrogel according to

these references, the body cavity would have to be subjected to ionizing radiation or reduced in temperature below 0°C.

- Tanihari discloses the use of a co-polymer, not a vinyl polymer, for use in a wound dressing. See Tests 2-3 and paragraph 5 of the Spiegelberg declaration (February 13, 2008). To obtain a hydrogel, Tanihara employed: (1) cross-linking with radiation or peroxides; (2) cooling the solution; (3) freezing of the solution; and (4) repetition of freezing and thawing. See column 20, line 15 of Tanihara. In additional, Tanihara methods require either chemical reaction of the polymer solution with an anhydride or taurine, or a freeze-thaw process. None of these approaches would allow for injectability.

In contrast to these references, the claimed invention requires none of these steps and, in fact, specifically recites "wherein the polymer hydrogel is formed without chemical crosslinkers, irradiation or thermal cycling." The invention provides for an injectable solution that will gel *in situ* to form the hydrogel without the need for deleterious treatments of the body.

Regarding the non-injectability of the prior art hydrogels, the examiner contends that the experiment as described in the first declaration (filed March 2, 2007) was not commensurate in scope with what is actually being claimed. In order to address the issue and to demonstrate that the none of the processes disclosed in the cited references yield "injectable hydrogel", applicant submitted the 2008 declaration of Dr. Stephen Spiegelberg, which is based on additional four experiments. These experiments demonstrate that solutions according to the invention are injectable and spontaneously form gel after injection. The experiments also provide proof that the

materials disclosed in the cited arts are not injectable. The data also support the claimed invention that the polymer hydrogel gels *in situ* after the injection without a further processing step. This is not possible using chemical cross-linking, radiation cross-linking, or thermal processing techniques to create the gels disclosed in the cited references (see 2008 Spiegelberg Declaration, Tests 1-4, for example).

The Federal Circuit has held that the citation of many references which skirt around the invention is indicative of patentability, not obviousness. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.,* 231 USPQ 81, 93 (Fed. Cir. 1986); *see generally In re Herrick*, 145 USPQ 400, 402 (CCPA 1965). Applicants submit that this principle applies here, and therefore urge that the rejections be withdrawn.

The claimed invention has unexpectedly improved properties and characteristics, and satisfies a long-felt but previously unmet need

As explained in paragraph 3 of the 2008 Spiegelberg declaration, the claimed invention unexpectedly provides and allows for (1) minimally invasive surgery, (2) a porous, highly hydrated system allows fluid and nutrient flow from endplates, (3) space-filling for optimal load-transfer to the annulus fibrosis, and (4) the absence of chemical action, so there are no unwanted chemical by-products or exothermic (heat) occurrences. This is achieved while satisfying the long-felt need for an injectable product. *See* MPEP § 2141.

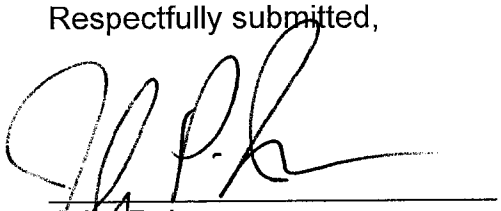
The attainment of unexpected results or properties is a powerful demonstration of patentability. *See U.S. v. Adams*, 383 U.S. 39, 51-52 (1966); *Lindemann Maschinenfabrik v. American Hoist and Derrick Co.*, 730 F.2d 1452, 1461 (Fed. Cir. 1984). Absent evidence to the contrary, applicants' demonstration of unexpected

results further establishes patentability. *See In re Soni*, 34 USPQ2d 1684, 1687-88 (Fed. Cir. 1995). Furthermore, The satisfaction of long-felt need constitutes further evidence of the patentability of the present invention. *See Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). These objective indicia of non-obviousness further demonstrate the patentability of the invention.

REQUEST

Applicants submit that claims 135-156 are in condition for allowance and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 416-6800 should there be any questions.

Respectfully submitted,



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